

Serial No. 09/847,935
Reply of March 17, 2006

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REMARKS

Applicants are in receipt of the Office Action mailed November 10, 2005, and have the following comments.

The Applicants cancelled claims 36, 39-41, 43-50, 53-59, 70, 71, 74-76 and 78-86 in the Reply dated August 22, 2005 in order to permit claims 60-66, 68, 72, 73 and 77, indicated as allowable, to proceed to issue. The Examiner has subsequently withdrawn the indication that these claims are allowable, and the Applicants therefore reserve the right to present any pending claim without prejudice, and the cancelled claims, without any estoppel having been created due to the cancellation.

Claim 1 has been amended to indicate that the efficiency enhancing component comprises a fatty acid. Support of this amendment can be found in the specification at, for example, Example 1 and page 4, second full paragraph. New claims 87-90 have been added; support for these claims can be found in, e.g., the claims as originally filed and the specification at page 6, first full paragraph.

Rejection pursuant to 35 USC §102(b)

The Office Action has rejected claims 60-63, 65, 66, and 68 as being allegedly anticipated by DeSantis, Jr. et al., U.S. Patent

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5,811,443. Applicants respectfully traverse this rejection for the following reasons.

Independent claim 60 is directed to a composition comprising an ion-paired complex comprising a therapeutic component comprising an alpha adrenergic agonist, and an efficiency-enhancing component (EEC), wherein the EEC comprises a fatty acid.

According to the November 20, 2005 Office Action, DeSantis discloses a composition comprising a clonidine derivative and at least one prostaglandin, wherein the composition may optionally comprise anionic mucomimetic polymers. The Office Action indicates that the anionic polymer is the EEC of the DeSantis, Jr. composition.

An invention is anticipated if each and every element of the claimed invention is disclosed in a single prior art reference. See, e.g., *In re Paulsen*, 30 F.3d 1475, 31 USPQ2d 1671 (Fed. Cir. 1994) (emphasis added). Moreover, this reference must disclose these elements either expressly or inherently, as well as structure which is capable of performing any recited functional limitations. *RCA Corp. v. Applied Digital Data Sys. Inc.*, 730 F.2d 1440, 1444; 221 USPQ 385, 388 (Fed. Cir. 1984). An anticipatory reference must place the person of ordinary skill in the art in possession of the claimed invention. *In re Spada*, 911 F.2d 705, ___, 15 USPQ2d 1655, 1657 (Fed. Cir. 1990); *Akzo Nobel, N.V. v. U.S. International Trade Commission*, 808 F.2d

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1471, 1479), 1 USPQ2d 1241, 1245 (Fed. Cir. 1986); In re Coker, 463 F2d 1344, 1348 (CCPA 1972).

The outstanding rejection is now moot, as anionic polymers are no longer claimed in claim 60 or any of the dependent claims, and prostaglandins are fatty acid derivatives, rather than fatty acids. Thus, the claims are free of 35 U.S.C. §102(b).

Rejection pursuant to 35 USC §102(e)

The Office Action has rejected claims 60-63, 65, 66, 68, 72 and 73 as being allegedly anticipated by Beck et al., U.S. Patent 6,358,935. Applicants respectfully traverse this rejection for the following reasons.

The Office Action alleges that Beck discloses compositions comprising a complex of brimonidine (an alpha 2 agonist) and cyclodextrins (which may comprise more than one anionic charge). Further, the Office Action alleges that carboxymethylcellulose, an optional ingredient in the compositions of Beck, may comprise "an additional EEC".

As above, these rejections are now moot in light of the amendment of claim 60 to specify the EEC as a fatty acid. For this reason Applicants submit the rejected claims are free of 35 U.S.C. §102(e).

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Rejection pursuant to 35 USC §103(a)

The Office Action has rejected claims 60-63, 65, 66, 72, 73, and 77 as being allegedly obvious over Gil et al., U.S. Patent No. 6,294,553. Applicants hereby respectfully traverse this rejection for the following reasons.

Gil is said to disclose compositions comprising brimonidine and, optionally, preservatives, stabilizers, penetration enhancers and/or vehicles; these ingredients may comprise oleic acid (a fatty acid), anionic surfactants, such as polyoxymers, and cellulose derivatives.

To establish a *prima facie* case of obviousness, an Office Action must first provide evidence of some suggestion or motivation to modify the references or to combine the reference teachings. Second, the Office Action must show that the person of skill in the art would have had a reasonable expectation of success if the suggestion were followed. Lastly, the prior art reference(s) must teach or suggest all the claim limitations. See e.g., Manual of Patent Examining Procedure (MPEP) § 2143.

Moreover, the mere fact that a reference is capable of being modified, or is even "well within the ordinary skill of the art" does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination. *Id.* at III

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& IV, citing *In re Mills*, 16 USPQ2d 1430 (Fed. Cir. 1990); *Ex parte Levengood*, 28 USPQ2d 1300 (Bd. Pat. App. & Inter. 1993).

The Office Action of November 20, 2005 correctly acknowledges that Gil does not disclose a concentration of an "efficiency-enhancing component"; this is because Gil does not suggest or disclose the "ion-pair complex", which is an element of all the pending claims.

The disclosure of Gil does not indicate an appreciation of the advantages of forming ion-pair complexes (such as the reduction in sedative effect in animals given 0.2% (w/v) of ion paired brimonidine/linoleic acid as compared to 0.2% brimonidine shown in e.g., Example 3, Table 1 of the present Specification). This deficiency compels the conclusion that, contrary to the assertions made in the November 20, 2005 Office Action, Gil does not in any way suggest or provide any motivation to a person of ordinary skill in the art to make compositions comprising brimonidine and, for example oleic acid, in such proportions as to comprise a charge-neutralizing molar ratio of the TC and the EEC, such that "ion pairs" comprising TC and EEC would be formed and the resulting complex be "provided with enhanced ability to cross a lipid membrane." Specification, paragraph bridging pages 5 and 6

Thus, the Office Action's statement on page 6 that "there is no demonstration in applicants' specification showing that efficacy enhancing component in amounts greater than 0.2% and less than 10% provides unusual results" respectfully misses the mark. It is the

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complexation of TC and EEC in particular molar ratios (see e.g., Specification at page 6, first full paragraph), rather than the specific concentration of an EEC, that effectively permits a reduction in overall charge. This reduction of overall charge thus permits the TC to pass more freely through lipid membranes. Also, these compositions provide lessened sedation relative to the same amount of the active ingredient. See, Example 3, Table 1 of the present specification. Therefore, contrary to the assertion quoted above, the specification shows that currently claimed compositions clearly do provide unusual results.

The Office Action clearly indicates that Gil does not suggest or teach the present invention as it indicates that since Gil "is silent on the amount of the efficiency-enhancing component, it would appear that all or a certain amount [of the EEC] would be suitable to provide the desired effect." Office Action, page 6. It is certainly true that Gil is silent on the amount of the EEC. It is also true, that Gil does not report any particular advantage with reader to the brimonidine compositions disclosed, in adding or leaving out any particular ingredient other than brimonidine, including oleic acid.

For these reasons Applicants respectfully submit that the Office Action of November 20, 2005 fails to establish a *prima facie* case of obviousness against the claimed compositions, and that the claims should therefore be allowed to proceed to issue.

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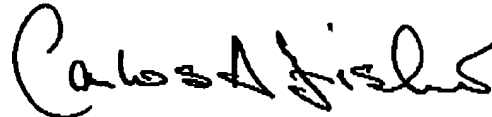
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CONCLUSION

No fee is thought to be due in connection with this communication, as it is being filed within the two month shortened statutory period for submitting an appeal brief. However, if Applicants are in error in this regard, kindly use Deposit Account 01-0885 for the payment of any charge now due.

Respectfully submitted,



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